Relationschip of PTEN mutations and EGFR amplification with p27 and cyclin D1 through Akt in glioblastomas

118. Subject: Abstract from Braintumormeetin
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title of abstract: RELATIONSHIP OF OTEN MUTATIONS AND EGFR AMPLIFICATION WITH p27 AND CYCLIN D1 THROUGH Akt IN GLIOBLASTOMAS
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abstract: Downstream PIP3 generation by PI-3 Kinase activates Akt which inactivates AFX/FKHR with the consequent decrease of p27/Kip.1 expression and enhancement of cyclin D1 expression. PTEN lipid phosphatase degrades PIP3 and negatively regulates Akt, whereas its loss abrogates the negative regulation of Akt which can thus suppress pro-apoptotic function of BAD and caspase-9. The same pathway can be followed by activation of PI-3 Kinase by EGFR. p27/Kip.1 has been certainly found down-regulated by deltaEGFR. In glioblastomas, especially in primary ones, PTEN is mutated in 27-40% of cases and EGFR amplified in 60-65% of cases.
PTEN mutations and EGFR amplification by PCR, Akt, p27/Kip.1 and cyclin D1 by immunohistochemistry with relevant antibodies and immunoblotting, apoptosis by TUNEL and LI of Ki.67 MIB.1 were studied in a series of 75 operated glioblastomas and compared among them and with survival. EGFR amplification and PTEN mutations were present in 40% and 30% respectively of glioblastomas and simultaneously in 7 cases. A relationship between EGFR amplification and PTEN mutations, evaluated separately, and p27/Kip.1 and cyclin D1 was not clearly found, not even in cases with both alterations together. For Akt we could not obtain till now reliable results. p27/Kip.1 and cyclin D1 are maybe also under other regulatory mechanisms.
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